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EXAMINER
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ART UNIT	PAPER NUMBER
185	3

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ___ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-39 are pending in the application.
   Of the above, claims 1-11, 14, 27-29, 31-34, 36-39 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 12-13, 15-26, 30 and 35 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev.9-89)

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-11, 14, 27-29, 31-32, and 36-37 drawn to metalloproteinase inhibitor protein, classified in Class 530, subclass 324.

II. Claims 12-13, 15-26, 30 and 35, drawn to DNA sequences, vectors and host cells, classified in Class 435, subclass 69.2.

III. Claims 33 and 34, drawn to a method of inhibiting metastasis and a method of treating arthritis, classified in Class 514, subclass 12.

IV. Claims 38 and 39, drawn to antibodies, classified in Class 530, subclass 387.

The inventions are distinct, each from the other because of the following reasons:

Inventions II and I are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (M.P.E.P. § 806.05(f)). In the instant case the product as claimed can be made by a materially different process such as chemical synthesis.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the

product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the protein may be used in inhibiting cancer metastasis, or in treating arthritis.

Inventions I and IV are chemically distinct entities and would support separate patents.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Henry Nowak on 9-13-91 a provisional election was made with traverse to prosecute the invention of Group II, claims 12-13, 15-26, 30 and 35. Affirmation of this election must be made by applicant in responding to this Office action. Claims 1-11, 14, 27-29, 31-34, and 36-39 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition

under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Applicant is encouraged to submit an Information Disclosure Statement including (1) a form PTO-1449, "Information Disclosure Citation" listing patents, publications and other information material to the instant application, (2) a concise explanation of the relevance of each listed item and (3) a copy of each listed item as a means of complying with the duty of disclosure set forth in 37 CFR 1.56. See 37 CFR 1.97 through 37 CFR 1.99, MPEP 609 and MPEP 2001.06 through 2004 for further guidance.

Claims 15-22, 25, 26 and 30 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the DNA sequences of the vectors p1156HMI2, pYEαG4-HMI and pDSFα2-MI which have been shown to express the metalloproteinase inhibitor protein as is necessary in these claims. Since the disclosure contains no teaching of what specific elements must be contained within a DNA sequence in order for it to be expressed in various hosts and because in the prior art, the expression of a protein in a foreign host is unpredictable (dependent on host cell factors, etc.), it appears that an undue amount of experimentation would be required for one of ordinary skill in the art to practice the invention with other DNA sequences. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Claims 12-13, 15-26, 30 and 35 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is

not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The scope of the claims is much broader than the specification is enabling for. The claims are replete with functional language and do not provide adequate structural information to properly define the invention. The functional language is vague and indefinite as well, since the language does not properly define the metes and bounds of the invention. It is not clear at all how broad the functional language is intended to cover. The phrases which are inadequately enabled or vague and indefinte and therefore objected to are as follows:

-In claims 12 (from which claims 13, 25, 26, and 30 depend), 15 (from which claims 16-22 depend) and 30, the phrases "primary structural conformation" and "biological properties";

-In claims 19 and 21, the phrase "including codons prefered for expression";

-In claim 23 (from which claim 24 depends), the phrase "polypeptide fragment";

-In claims 23 and 35, the phrase "polypeptide analog";

-In claim 25, the phrase "biologically functional".

The limitations of all of the above phrases are subject to individual interpretation and could be construed in very narrow to very broad terms.

Claim 30 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim is indefinite in the recitation of : "products of the expression of DNA sequences in". as the products could be any protein expressed by the host as well as metalloproteinase inhibitor. Replacement with "products of the expression of said DNA sequences" would clarify the meaning.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12-13, 15-16, 18, 23-26, 30 and 35 are rejected under 35 U.S.C. § 102(b) as being anticipated by Docherty et al. Docherty et al. disclose the cDNA sequence and vectors for expression of TIMP and cells transformed by these vectors. As the sequence of TIMP contains a stretch of 8 amino acids (#'s7-14) in common with metalloproteinase inhibitor containing only a single mismatch as well as several other shorter stretchs of homology, this sequence would meet all of the limitations of the above claims. In regards to claim 15 (and those claims which depend on it) if applicant intends "the primary structural conformation" to mean only the <u>entire</u> and

exact amino acid sequence of metalloproteinase inhibitor, then this must be stated in clear, concise and unambiguous terms. Otherwise, since the disclosure contains no teaching on what parts of the metalloproteinase inhibitor sequence must be different from the sequences of related proteins such as TIMP, all such proteins must be considered to have the primary structural conformation of metalloproteinase inhibitor.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not

commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 12-13, 15-16, 18, 20, 23, and 25 are rejected under 35 U.S.C. § 103 as being unpatentable over Murray et al in view of Kimmel. Murray et al. disclose a metalloproteinase inhibitor of bovine origin with an amino terminal amino acid sequence essentially identical to that of metalloproteinase inhibitor. Kimmel shows procedures for the isolation of a cDNA sequence from a known amino acid or nucleotide sequence. Therefore it would have been obvious to one of ordinary skill in the art to isolate the DNA sequence corresponding to the protein of Murray et al. in order to express the protein in other hosts.

Claim 17 is rejected under 35 U.S.C. § 103 as being unpatentable over Docherty et al. taken alone or over Murray et al. and Kimmel both in view of Dilella and Woo. Docherty et al. or Murray et al. and Kimmel disclose a cDNA sequence of the protein as claimed. Dilella and Woo disclose a method of isolating genomic DNA sequences corresponding to an isolated cDNA sequence. As this method is applicable to any cDNA sequence it would have been obvious to use this method to obtain the genomic DNA corresponding to the cDNA of Docherty et al. or Murray et al. and Kimmel.

Claims 19 and 21 are rejected under 35 U.S.C. § 103 as being unpatentable over Docherty et al. taken alone or over Murray et

al. and Kimmel both in view of Robinson et al. and Bennetzen et al. Docherty et al. or Murray et al. and Kimmel disclose a cDNA sequence of the protein as claimed. Robinson and Bennetzen disclose that proteins expressed in high levels in E.coli and yeast contain higher levels of particular codons for certain amino acids and that codon selection can effect the level of translation of a protein. Therefore, it would have been obvious to one of ordinary skill in the art to substitute one or more of the codons found by Robinson and Bennetzen to be present in efficiently translated messages for the codons of the cDNA of Docherty et al. or Murray et al. and Kimmel to increase the level of translation of the protein.

Claim 22 is rejected under 35 U.S.C. § 103 as being unpatentable over Docherty et al. taken alone or over Murray et al. and Kimmel both in view of Gebeyehu et al. Docherty et al. or Murray et al. and Kimmel disclose a cDNA coding for a protein as claimed. Gebeyehu et al. disclose a method of biotin labeling of DNA. As the method can be used to label any DNA, it would have been obvious to one of ordinary skill in the art to use the method of Gebeyehu et al. to biotin label the cDNA of Docherty et al. or Murray et al. and Kimmel to take advantage of the ease and safety of biotin detection to isolate sequences of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, whose telephone number is (703) 308-4205.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196

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SUPERVISORY PATENT EXAMINER
ART UNIT 185